some yeast species (and some bacteria and plants as well) synthesize and excrete huge quantities of RF under iron limitation conditions. Mechanisms of such regulation and physiological role of this phenomenon are poorly understood. Yeast mutants which flavinogenic activity does not depend on the iron content in the medium were obtained. RF transport (both uptake and excretion) have been studied in *Saccharomyces cerevisiae*, the flavinogenic yeast *Pichia guilliermondii*, and to a lesser extent the flavinogenic fungus *Ashbya gossypii*. Several genes encoding putative RF excretase were identified in *P. guilliermondii* and *Debaryomyces hansenii* genomes by searching for homology to human BCRP1 (Breast Cancer Resistant Protein) that was identified as a RF excretase. It can be assumed that facilitating the extrusion of vitamin and blocking its absorption can be used to increase its production. Particular attention deserves the search for ways to increase the excretion of flavin by natural and artificially-created yeast overproducers. *Candida famata* yeasts are considered to be the most promising model of this research because of the ability to RF and FMN overproduction. The excretase genes of this yeast not identified due to the lack of genome sequencing data. Increasing the flavins excretion by *C. famata* cells may be achieved by the inserting of the excretase gene which was identified in the genetically close *D. hansenii* genus.

The aim of this work was to achieve the heterologous expression of the RF excretase gene *BCRP*1, in the RF and FMN overproducers *C. famata* AF4, *#91* and FMN-13 yeast strains.

In this work, we used standard molecular genetic techniques. Genomic DNA was isolated from yeasts using Wizard® Genomic DNA Purification Kit (Promega, Madison, WI, USA). Polymerase chain reaction (PCR) was performed on Thermocyclers GeneAmp® PCR System 9700 (Applied Biosystems, Foster City, CA, USA) using Platinum® Taq DNA Polymerase High Fidelity (Invitrogen, Carlsbad, CA, USA) according to manufacturer's instructions. *D. hansenii* excretase gene was amplified by PCR using BamHI and PstI (ExFrw: cgcGGATCCatgatatctataagtaacccaatg, ExRew: aaaCTGCAGtcactttctcaactttaaaccaac, PCR product size - 1857 bp) primers for further cloning of this fragment in yeast integrative pUC57_TEF1_ble plasmid. Restriction enzyme and ligase were used according to manufacturer's instructions (Fermentas, Vilnius, Lithuania). Isolation of plasmid DNA from *Escherichia coli* bacteria was performed using Wizard® Plus SV Minipreps DNA Purification System (Promega, Madison, WI, USA). Transformation of yeast *C. famata* was carried out by electroporation.

Yeast integrative pUC57_TEF1_BCRP1_ble plasmid which contained *D. hansenii* RF excretase *BCRP*1 gene under the control of the *TEF*1 promoter of the same yeast strain was constructed, XhoI-linearized and transformed into *C. famata* strains. As a selective marker *Staphylococcus aureus ble* gene, which protein product provides resistance to phleomycin for *E. coli* and *C. famata* was used. 30 transformants resistant to phleomycin were received. All types of transformants were stabilized by cultivation in non-selective media for 10–12 generations with further shifting to the selective media containing appropriate selective agents. The presence of the corresponding gene in the stabilized transformants was confirmed by diagnostic PCR.

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NANOCOMPOSITE MATERIALS: PERSPECTIVES ON THE USE AS INHIBITORS OF STAPHYLOCOCCAL ADHESION

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Staphylococcus aureus is an opportunistic pathogen which is a natural inhabitant of human microflora. Numerous different adhesins are represented at the bacterial surface; they provide the staphylococcal cells with the ability to attach to both abiotic and biotic surfaces. Concerning it, staphylococci may spread around human organs and liquids, as well as at surfaces of medical devices. Moreover, adhesion is a crucial step in the process of biofilm formation. For this reason,

the inhibition of latter prevents the development of an infectious process. In this regard, the use of nanocomposite materials may be prospective in order to reduce the adhesion of the bacterial cells to human ones. Such cutting-edge approach may decrease mortality and morbidity rates in future.

For this reason, two types of nanocomposite material have been used in the study: dispersed silica and ornidazole nanocomposite from alcoholic solution (DPSONAS) of the concentrations 2 and 4 %, and functionalized TA mirchospheres with absorbed ions of Cu^{2+} (fTACu) and without them (TA) of the concentration 0.1 and 0.01 % during a two-hour contact with bacterial cells. The adhesion of bacterial cells was studied using native erythrocytes of OO, AO, BO, AB blood types and standartized cell suspensions of daily cultures of *S. aureus* ATCC 25923 and two isolates of *Staphylococcus sp*. R1 and R2 from animals with the concentration of 0,5 McFarland units due to Brillis method [Minukhin, 2013].

It was estimated that according to the scale of numerical values all of the examined strains belong to high-adhesive (IAM > 4.0). The IAM for *S. aureus* ATCC 25923 was 6.2, and 8.23 and 6.17 for *Staphylococcus* sp. R1 and R2, respectively. In terms of the study, the inhibitory effect on adhesion of DPSONAS using *S. aureus* ATCC 25923 and fTACu and fTA using isolates R1 and R2, the reduced adhesion to native erythrocytes of human blood has been shown. In case of fTACu and fTA, comparing to DPSONAS, more significant impact on adhesion has been observed. However, concentration-based dependence was not observed. It was also revealed that the effect differed depending on the blood type. While using the OO blood type adhesion was reduced by 18 and 44 % at 2 and 4 %. In the case of AB blood type, the inhibitory effect was also present, but the adhesive activity was decreased by 9 and 18 %. Using AO and BO blood types it was shown that the inhibition of adhesion was more effective at 2% concentration in comparison to 4 % solution. The adhesion was reduced by 12 % in case of AO blood type and by 51 % in case of BO blood type. In comparison the use of 4 % solution decreased adhesion by 5 and 21 %.

In the study, the difference between the ability of animal isolates to adhere to RBC of AO blood type has been observed. For R1 and R2, it was 7.2 and 4.2, respectively. The use of the nanocomposites of another configuration has proved effective in both animal isolates. fTA has been shown to possess more efficient inhibitory of R1's adhesion in both concentrations (63 and 68 %) rather than fTA Cu (50 and 47 %). In R2, however, the effect was opposite. Regardless the concentration, fTACu was more active (50 and 62 %) than fTA (40 and 25 %).

Therefore, the findings of the study show the anti-adhesive effects of dispersed and functionalized nanocomposites against *S. aureus* ATCC 25923 and animal isolates. They also estimate that nanocomposites may be prospective in order to prevent the development of staphylococcal infections in clinical settings.

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CORRECTION OF VAGINAL MICROBIOTA WITH PROBIOTICS IN THE CASE OF MIXED BACTERIAL UROGENITAL TRACT INFECTION

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It is known that dysbiotic disorders of genitourinary system microbiota, primarily of the vagina, are the basis for development of infectious and inflammatory diseases, often induced by aggressive forms of opportunistic microorganisms (staphylococci, streptococci, *Candida* species, etc.) [Stapleton, 2016; van de Wijgert, 2016; Jespers, 2017]. The results of many studies substantiated the feasibility of using probiotics based on the commensal microbiota of human mucous